REMARKS

In the Office Action dated March 21, 2007, Claims 1-19 are pending and under examination. Claim 17 is rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Claims 1-8, 13-19 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support. Claim 15 is rejected under 35 U.S.C. §102(e) as allegedly anticipated by Falsen et al. (*Journal of Systematic Bacteriology*, 217-21, 1999).[1] Claims 1-14, and 18 are rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-17 of U.S. Patent No. 6,479,051, in view of Falsen et al. and Nugent et al., (*J. Clin Microbiol.* 29: 297-301, 1991). Claims 1-14, and 17 are rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-17 of U.S. Patent No. 6,479,051, in view of Falsen et al. and Nugent et al. and further in view of Gibson et al., (*Gastroenterology*, 975-82, 1995). Claims 1-15 are rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1, 2, 5, 6, 7, 8, 9 and 10 of U.S. Patent No. 6,180,100, in view of Falsen et al. and Nugent et al.

This Response addresses each of the Examiner's rejections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

With respect to the previously submitted election, the Examiner acknowledges urogenital flora as specifically named bacterial flora, *L. rhamnosus* as specifically named second probiotic organism and oral administration as specifically named method of administration.

The Examiner maintains the restriction requirement in view of Applicants' argument in the previous response. In this regard, with respect to the Examiner statement on page 2 of the

[1] Applicants note that the Examiner cites 35 U.S.C. §102(b) in the Office Action and the cited art is a published article, not patent or patent application. Thus, Applicants believe that the proper rejection should be 35 U.S.C. §102(b).

Official Action, Applicants submit that the Examiner correctly states that the urogenital and intestinal microbiota comprise different bacterial types. However, Applicants submit that of relevance to this application, both regions of the body do comprise *L. iners*, and indeed the intestine is the source of these organisms for the urogenital tract. Moreover, Applicants wish to bring the Examiner's attention to the fact that scientists have recently reported the presence of *L. iners* in both the intestine and vagina, and confirm that it is present in different populations of women at different life stages. See, e.g., Ferris et al., "Cultivation-independent analysis of changes in bacterial vaginosis flora following metronidazole treatment," *J Clin Microbiol.* 2007 Mar;45(3):1016-8; Anukam et al., "Lactobacillus vaginal microbiota of women attending a reproductive health care service in Benin city," *Nigeria. Sex Transm Dis.* 2006 Jan;33(1):59-62; Hill et al., "Characterization of vaginal microflora of healthy, nonpregnant women by chaperonin-60 sequence-based methods," *Am J Obstet Gynecol.* 2005 Sep;193(3 Pt 1):682-92; Devillard et al., "Novel insight into the vaginal microflora in postmenopausal women under hormone replacement therapy as analyzed by PCR-denaturing gradient gel electrophoresis," *Eur J Obstet Gynecol Reprod Biol.* 2004 Nov 10;117(1):76-81; and Zhou et al., Forney LJ. "Characterization of vaginal microbial communities in adult healthy women using cultivation-independent methods," *Microbiology* 2004 Aug;150(Pt 8):2565-73. Applicants are willing to submit copies of these references upon request by the Examiner. Thus, Applicants respectfully submit that these organisms are important in the function of the intestine and urogenital tract throughout life.

Applicants submit that it is extremely difficult, if not impossible, to eradicate an indigenous bacterial constituent after the first year or so of life when the flora develops, unless massive doses of antibiotics are used. Applicants submit that even when massive doses of antibiotics are used, once the antibiotics are stopped, the patient's flora often returns. Thus,

Applicants respectfully submit that the consistent wide-ranging finding of *L. iners* demonstrates clearly its fundamental presence in healthy people of all ages. Applicants respectfully request the Examiner to reconsider the restriction and examine all the strains together.

The Examiner alleges that the present invention is drawn to a method for establishing a healthy vaginal bacterial flora in females by administration of a therapeutically effective amount of at least one *Lactobacillus iners* in a pharmaceutically acceptable carrier. Moreover, the Examiner states that the present invention is to the administration of an additional second probiotic organism.

Claim 17 is rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. The Examiner states that Claim 17 claims insulin as a prebiotic. The Examiner states that it is unclear how insulin relates to insulin as a prebiotic.

Applicants have amended Claim 17 to recite "inulin." Support for the amendment is found in submit that the recitation For the purpose of a compact prosecution, the prebiotic claimed in claims 17 is interpreted as "inulin". Support for the amendment to Claim 17 is found on page 7, lines 5-9 and page 16, lines 12-14. No new matter is introduced by the amendment. Applicants submit that Claim 17, as amended, is clear and not indefinite. As such, the rejection of Claim 17 under 35 U.S.C. §112, second paragraph, is overcome and withdrawal thereof is respectfully requested.

Claims 1-8 and 13-19 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support. The Examiner acknowledges that the specification is enabling for a method of inhibiting urogenital pathogen colonization of the urogenital tract in women comprising orally administering a therapeutically effective amount of at least one *Lactobacillus iners* and a pharmaceutically acceptable carrier (emphasis added). However, the Examiner alleges that the specification does not reasonably provide enablement for a method of

maintaining a healthy urogenital flora in females by administering a therapeutically effective amount of at least one *L. iners* by any route of administration (emphasis added).

Before addressing the merits of the present rejection, Applicants have added Claim 20, which is directed to a method for inhibiting and displacing vaginal pathogens by administering a therapeutically effective amount of at least one *Lactobacillus iners* and a pharmaceutically acceptable carrier. Support for Claim 20 can be found throughout the specification, e.g., at page 10, last paragraph. As mentioned above, the Examiner acknowledges the enabling support of the present application for a method of inhibiting urogenital pathogen colonization of the urogenital tract in women. Applicants submit that a "method of inhibiting" refers to reducing the chances of an infection occurring. Applicants submit that the word "displacing" refers to disrupting an existing infectious nidus and thereby treating an infection. The enablement of Claim 20 is further evidenced by Saunders et al., "Disruption of Gardnerella vaginalis biofilms by Lactobacillus," *Coll. Surf. B: Biointerfaces* 2007: 55: 138-142. Figures 3, 4 and 8 from Saunders et al. are attached as **Exhibits A, B and C**.

Applicants submit that the *L. iners* inhibits the ability of the uropathogens to adhere and colonize in the urogenital tract, following oral administration. Applicants respectfully submit that if *L. iners* did not inhibit the ability of the uropathogens to adhere and colonize in the urogenital tract, *L. iners* itself would not be able to be sustained in the vagina. Indeed, *L. iners* is commonly the dominant *Lactobacillus* species in the vagina, i.e., *L. iners* is able to survive and flourish in the vagina. Applicants respectfully submit that the description in the specification makes it clear to those skilled in the art that they must administer a therapeutically effective amount of the *L. iners*. The specification provides that the organism could be administered in tablet, capsule, food or other form, in varying amounts depending on how each delivery system works.

The Examiner alleges that Claims 1-8 and 13-19 encompass a method for maintaining a healthy urogenital flora in females by administering a therapeutically effective amount of at least one *L. iners* by any route of administration, including parenteral (e.g., intramuscular, intracardiac, subcutaneous, intraperitoneal, intravenous), topical, and enteral (e.g., mouth) routes (emphasis by the Examiner).

In an effort to favorably advance prosecution, Applicants have amended Claims 1-8 and 13-19. Claims 1-8 and 13-19, as amended, recite the administration of *L. iners* via only oral and vaginal routes. However, Applicants submit that the method of delivery can vary, for example, in form of capsules, pads, or creams.

The Examiner alleges that Claim 19 encompasses methods for treatment of any infection in a subject, including a human subject. The Examiner alleges that the present application has only provided a limited *in vivo* characterization of the improved understanding of the bacterial vaginal flora of a woman before and after probiotic instillation with capsules of *L. rhamnosus* GR-1 and *L. fermentum* RC-14; and further contemplating the advantages of a combination therapy in some women for clinical studies of the vaginal tract. Thus, the Examiner alleges that Claim 19 lacks enabling support because of unpredictability of the art and the lack of working example in the specification.

The Examiner appears to believe that the administration of *L. iners* is only effective for human disease related to infections in the vaginal tract. In this regard, Applicants submit that probiotic *lactobacilli* have been shown to provide benefits to the respiratory and urinary tracts, after oral administration. Thus, Applicants respectfully submit that the present invention recognizes that *L. iners* can provide similar benefits. Applicants submit that although no prior art disclose that *L. iners* can achieve this specific effect to the respiratory and urinary tracts, evidence does exist in support of the effectiveness of administering *L. iners* for treatment of

diseases other than vaginal tract infections. For example, a recent study has shown that probiotic *lactobacilli* can boost the CD4 count in HIV/AIDS patients (Anukam et al. Yogurt containing probiotic Lactobacillus rhamnosus GR-1 and L. reuteri RC-14 helps resolve moderate diarrhea and increases CD4 count in HIV/AIDS patients. *J. Clin. Gastroenterol.* 2007; *in press*.). Other studies have shown that *lactobacilli* might reduce the risk of Chlamydia and herpes infections (Cherpes et al., Association between acquisition of herpes simplex virus type 2 in women and bacterial vaginosis. *Clin Infect Dis.* 2003 Aug 1;37(3):319-25 and Ness et al., Sweet RL, Rice P, Richter HE. Bacterial vaginosis (BV) and the risk of incident gonococcal or chlamydial genital infection in a predominantly black population. *Sex Transm Dis.* 2005 Jul;32(7):413-7). Applicants submit that given the ability of these organisms to modulate inflammation, it is also highly possible to use *lactobacilli* to treat or prevent cancers. In addition, Applicants submit that Claim 19, as written, does not exclude *L. iners* being co-administered with anti-virals or antibiotics or other medications. Indeed, a study by the inventors' group has recently shown that probiotic *lactobacilli* augment the efficacy of antibiotics in treating infection (Anukam et al., Augmentation of antimicrobial metronidazole therapy of bacterial vaginosis with oral probiotic Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14: randomized, double-blind, placebo controlled trial. *Microbes Infect.* 2006 May; 8(6): 1450-4). Applicants respectfully submit that Claim 19 is not directed to curing diseases, but to treating diseases, which subject matter is sufficiently supported by the disclosure of the present application, to one skilled in the art.

The Examiner mentioned a study of 19 women on pages 7-8 of the Official Action. Applicants respectfully submit that the study of 19 subjects simply shows the high prevalence of *L. iners*. It is not a citation about infection. Applicants submit that several other papers from the inventors' group have shown the ability of probiotic *lactobacilli* to treat infections (e.g., Anukam

et al. Clinical study comparing probiotic Lactobacillus GR-1 and RC-14 with metronidazole vaginal gel to treat symptomatic bacterial vaginosis. *Microbes Infect.* 2006 Oct; 8(12-13): 2772-6 and Reid G et al., Probiotic Lactobacillus dose required to restore and maintain a normal vaginal flora. *FEMS Immunol Med Microbiol.* 2001 Dec;32(1):37-41).

Therefore, Applicants respectfully submit that in view of the present application, one skilled in the art can utilize the appropriate *lactobacilli* in the methods as claimed in the present application, without undue experimentation. In view of the foregoing argument and the amendment to the claims, the rejection of Claims 1-8 and 13-19 under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support, is overcome and withdrawal thereof is respectfully requested.

Claim 15 is rejected under 35 U.S.C. §102(b) as allegedly anticipated by Falsen et al. (*Journal of Systematic Bacteriology*, 217-21, 1999).

The Examiner alleges that Claim 15 is directed to a pharmaceutical composition comprising *L. iners* and a pharmaceutically acceptable carrier. The Examiner alleges that the pharmaceutical composition can be broadly interpreted as any media that comprises *L. iners* without affecting the efficacy of the composition.

The Examiner alleges that Falsen et al., teaches a new isolated species of *Lactobacillus*: *L. iners* that grows in an agar culture supplemented with 5% horse blood at 37°C in air plus CO_2. Moreover, the Examiner alleges that the preparations of whole protein extract comprising *L. iners* is used for densitometric analysis (p. 218, col. 1).

Applicants respectfully submit that the claimed pharmaceutical composition does not include a growth medium as described by Falsen et al. On the contrary, the goal of the recited carrier is not to make the *L. iners* grow, but rather to retain its viability from the time of manufacture to use in the human.

However, in an effort to favorably advance prosecution, Applicants have incorporated the subject matter of Claim 16 into Claim 15. Claim 15, as amended, recites *L. iners*, a prebiotic and a pharmaceutically acceptable carrier. Applicants have also canceled Claim 16 and amended Claims 17-19 to depend upon Claim 15.

Applicants respectfully submit that nowhere does the Falsen et al. reference disclose a pharmaceutical composition comprising *L. iners*, a prebiotic and a pharmaceutically acceptable carrier. Therefore, the rejection of Claim 15 under 35 U.S.C. §102(b) as allegedly anticipated by Falsen et al. is overcome and withdrawn thereof is respectfully requested.

Claims 1-14, and 18 are rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-17 of U.S. Patent No. 6,479,051, in view of Falsen et al. and Nugent et al., (*J. Clin Microbiol.* 29: 297-301, 1991). Claims 1-14, and 17 are rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-17 of U.S. Patent No. 6,479,051, in view of Falsen et al. and Nugent et al. and further in view of Gibson et al., (*Gastroenterology*, 975-82, 1995). Claims 1-15 are rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1, 2, 5, 6, 7, 8, 9 and 10 of U.S. Patent No. 6,180,100, in view of Falsen et al. and Nugent et al.

Applicants respectfully submit that contrary to the Examiner's allegation, the delivery of *L. iners* in any form as a probiotic to prevent and treat urogenital infection, has not previously been suggested in U.S. Patent No. 6,479,051 or Falsen et al. 1999 or Nugent et al. 1991. The '051 patent discloses the delivery of *lactobacilli* by mouth for urogenital health. This is simply a delivery system, just as intravenous delivery of a drug is a system. Since *L. iners* had not been discovered when that the '051 patent was filed, there is no way the patent could suggest the invention disclosed in the present application. Applicants submit that the Falsen et al. reference

simply states that *L. iners* was discovered in vaginal samples. In its introductory comments, Falsen et al. simply put into context what *lactobacilli* are, and how they have been used. The reference does not describe oral or vaginal use of probiotics, let alone suggest or imply the present invention. For example, *L. vaginalis* was first discovered in 1989, as noted in the Falsen et al. reference. However, there are no probiotic products using this species.

To further illustrate that one skilled in the art would not automatically consider *L. iners* for oral or vaginal probiotic applications, an expert in this area, Dr. Ferris and his colleagues have stated recently (in March 2007) that "*L. iners* is prevalent in grade Ib, a variant of normal, and in grade III, representing bacterial vaginosis (BV). We speculate that *L. iners* is a transitional species and that an L. crispatus-predominant species composition represents a stable flora." (Ferris et al., Cultivation-independent analysis of changes in bacterial vaginosis flora following metronidazole treatment. *J Clin Microbiol.* Mar; 45(3):1016-18, 2007). Applicants respectfully submit that, in other words, one skilled in the art does not believe that *L. iners* would be a good choice of a probiotic. Applicants respectfully submit that since only the inventors' group has actually performed experiments using *L. iners*, the Ferris et al. reference is the first to evaluate *L. iners* in light of its probiotic potential. Applicants submit that Ferris et al.'s comments counter the Examiner's suggestion that it would be obvious for people skilled in the art to suggest that *L. iners* should be a probiotic as outlined in the present application. Applicants submit that contrary to the Examiner's allegation, it would be obvious <u>not to use</u> it in this way. Furthermore, Applicants respectfully submit that the fact that *L. iners* is so difficult to isolate, identify and grow (demonstrated by how long it has taken scientists to discover it in comparison to other vaginal *lactobacilli*), it would also <u>not</u> be obvious to study this species, and then apply it to humans.

Applicants submit that the Nugent reference is simply a description of a method to diagnose bacterial vaginosis using a Gram stain. Applicants submit that it has long been known that *lactobacilli* are associated with health and Nugent's studies do not contribute meaningfully to this area. Indeed, Applicants submit that *Atopobium vaginae* is a Gram positive rod shaped organism that could well be the one identified by Nugent as "normal", and yet it is associated with bacterial vaginosis (Burton et al. Detection of Atopobium vaginae in postmenopausal women by cultivation-independent methods warrants further investigation. *J Clin Microbiol.* Apr;42(4):1829-31, 2004). Thus, Nugent's slides and conclusions are equivocal, at best.

Applicants respectfully submit that it would not be obvious to have inulin added as a prebiotic to the preparation. Applicants submit that it is well known to one skilled in the art, not all *lactobacilli* grow in every prebiotic, which can be illustrated in the study of Rousseau et al. (Rousseau et al. Prebiotic effects of oligosaccharides on selected vaginal lactobacilli and pathogenic microorganisms. *Anaerobe.* Jun;11(3):145-53, 2005, e.g., as shown in the 3.7 section (attached as **Exhibit D**). Applicants respectfully submit that even assuming, *arguendo*, that studies prior to the present application had shown that inulin stimulated *lactobacilli* (rather than bifidobacteria – a completely different organism not part of the present invention), studies would have to have been done on *L. iners* to determine whether it would stimulate it's growth. However, Applicants respectfully submit that in the Rousseau et al. reference, the normal test was to use MRS broth for such studies. Applicants submit that in that case, *L. iners* would not have grown. Therefore, Applicants respectfully submit that no prior art discloses or suggests inulin being added to *L. iners*.

Applicants respectfully submit that the Examiner draws upon studies that are ten years apart, one on bacterial vaginosis diagnosis, one on specific *lactobacilli* strains stated in a patent, and one on the discovery of a new organism, to allege that it was obvious to one skilled in

the art to conclude that *L. iners* would be a good probiotic for urogenital health. However, Applicants respectfully submit that the Examiner's allegation is not supported by the situation of the state-of-the-art at the time of filing of the present application. On the contrary, the first experiment reported on the use of *L. iners* as a possible urogenital probiotic was in 2007 by the inventors' group (Saunders et al., "Disruption of Gardnerella vaginalis biofilms by Lactobacillus," *Coll. Surf. B: Biointerfaces* 2007: 55: 138-42 and Exhibits A-C). These experiments, as mentioned above, illustrate for the first time, the ability of *L. iners* to disrupt pathogenic biofilms found in bacterial vaginosis. Thus, Applicants respectfully submit that the Examiner cannot support his position of obviousness.

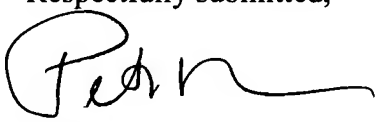
Moreover, Applicants respectfully submit that just because one *E. coli* strain causes urinary tract infection, does not mean that the same strain causes diarrhea. On the contrary, there is no such overlap – strains are uropathogenic, or enterotoxigenic, or some are even avirulent and beneficial to the host. Likewise, *L. reuteri* produce bacteriocins called reuterin (Talarico and Dobrogosz, Chemical characterization of an antimicrobial substance produced by Lactobacillus reuteri. *Antimicrob Agents Chemother* May;33(5):674-9, 1989), whereas *L. rhamnosus* do not. Applicants respectfully submit that the above argument does not intend to negate the importance of the discovery of *L. iners*. Rather, Applicants disagree with the Examiner's allegation that the present invention is obvious in view of the cited art.

In summary, Applicants respectfully submit that the novelty and non-obviousness of the present invention is multi-focal. The Examiner has failed to uncover any prior art that states that *L. iners* should be used as a probiotic, administered orally or vaginally, to restore and maintain health in the urogenital tract of women. Applicants note that it was not until September 15, 2005, much later than the present application was filed, that P&G filed two PCT applications on a similar use of L. *iners* and inulin (WO 2006/033951 and WO 2006/033950).

Therefore, Applicants respectfully submit that the present invention is not obvious in view of the cited art. The several obviousness-type based double patenting rejections are overcome and withdrawal thereof is respectfully requested.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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Encls.: Exhibits A-D

Figure 3. The effect on biofilm surface area for viable and dead bacteria, of challenging a *Garderella* biofilm with *Lactobacillus reuteri* RC-14 (2), *L. rhamnosus* GR-1 (3), *L. iners* AB-1 (4) and *L. crispatus* 33820 (5) compared to unchallenged control (1). Data represents average of 6 experiments; distribution was <20%.

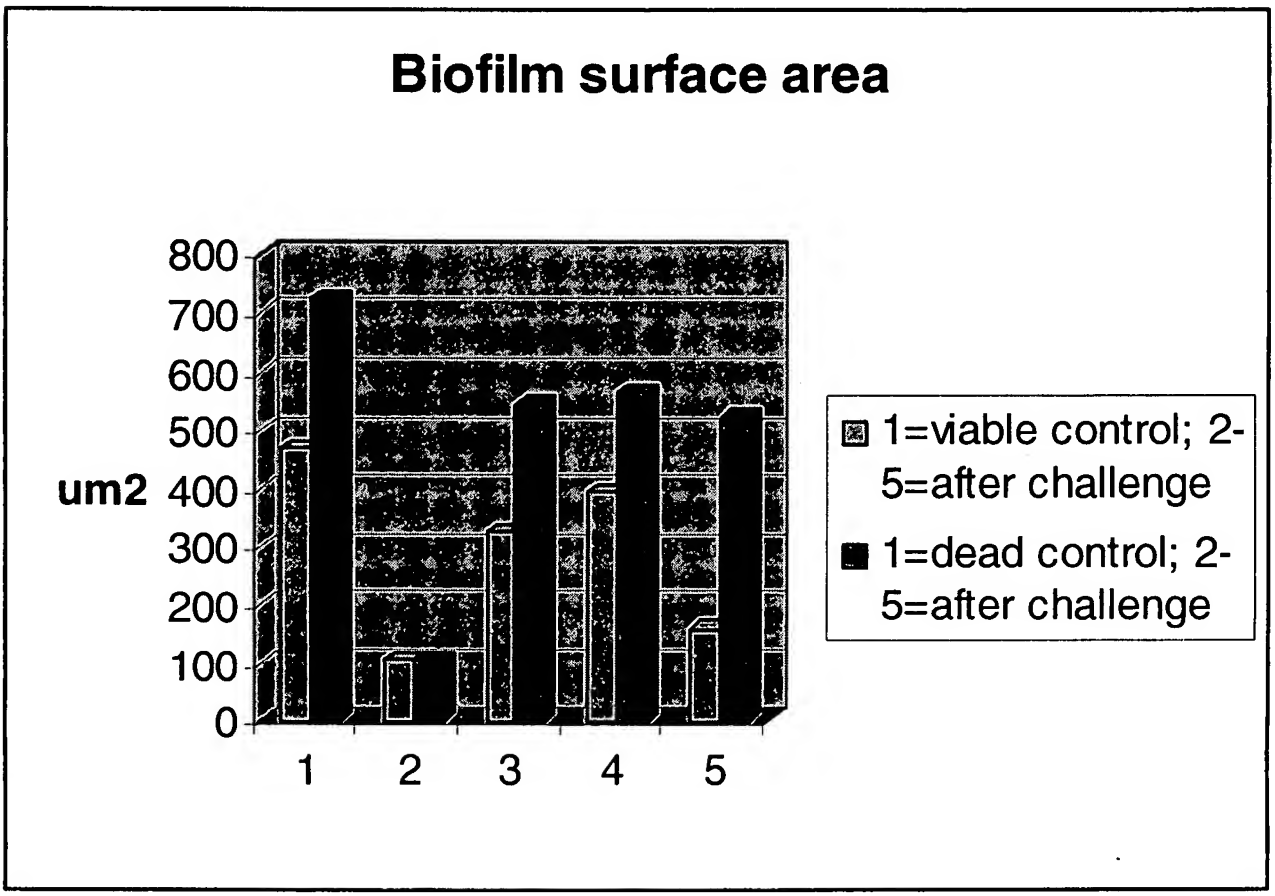


Figure 4. The effect on biofilm depth for viable and dead bacteria, of challenging a *Garderella* biofilm with *Lactobacillus reuteri* RC-14 (2), *L. rhamnosus* GR-1 (3), *L. iners* AB-1 (4) and *L. crispatus* 33820 (5) compared to unchallenged control (1). Data represents average of 6 experiments; distribution was <20%.

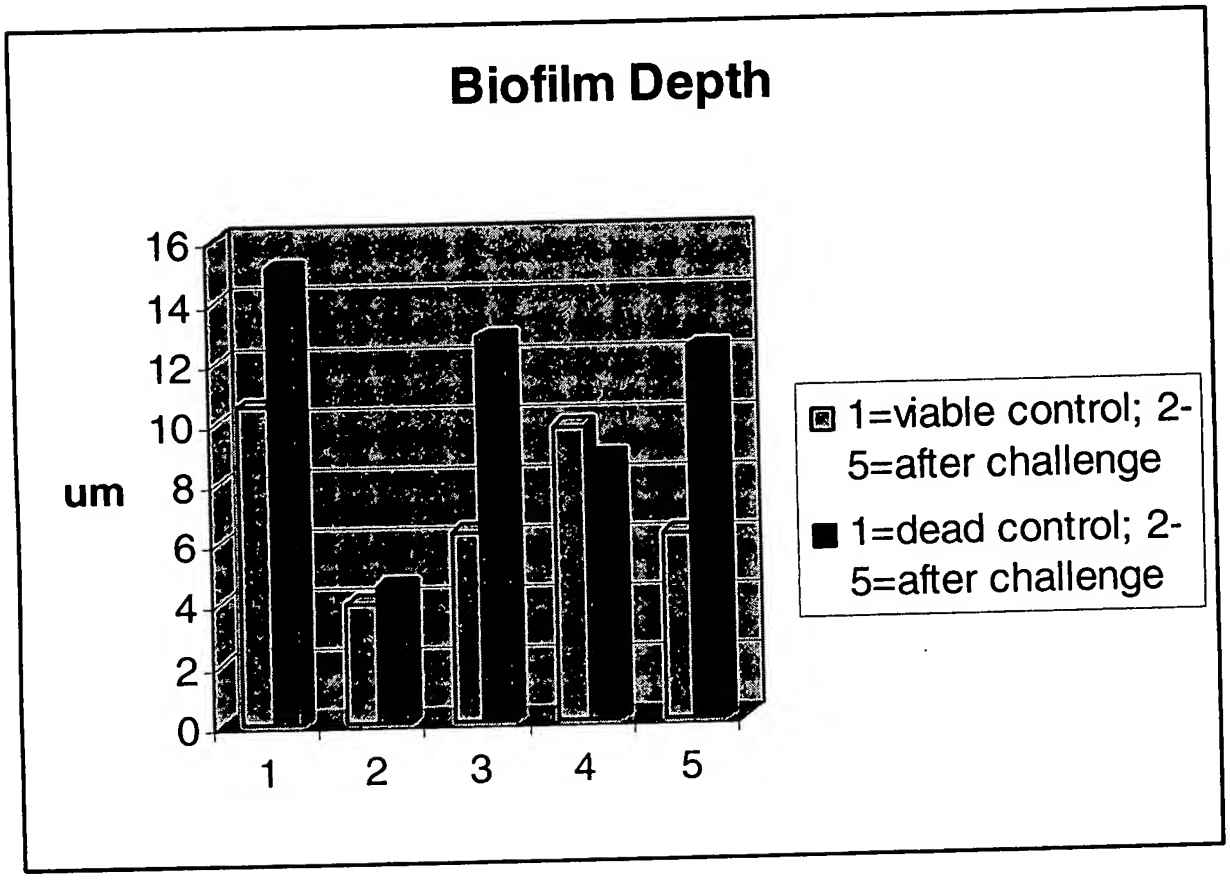
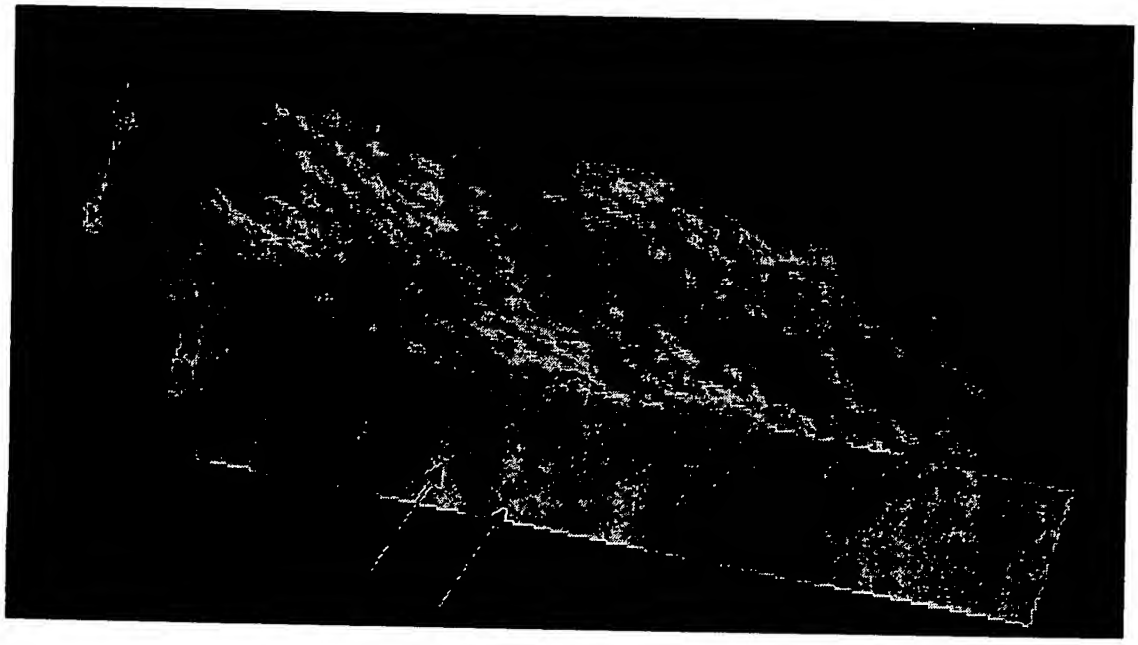


Figure 8. The samples challenged with *L. iners* AB-1 showed evidence of penetration of biofilm pods (red arrows), but less deep green viable cells compared to *L. rhamnosus* GR-1 (Figure 7), perhaps due to the fastidious nature of the organisms.



3.7. Vaginal lactobacilli growth on oligosaccharide carbon source

Controls for the lactobacilli were carried out on MRS broth containing either glucose or no carbohydrate. The turbidity at 640 nm after 48 h incubation on glucose medium ranged from 0.40 to 0.60 depending on the strain. The growth in the absence of carbon sources was very low as indicated by the turbidity, which remained lower than 0.05 for all the strains. The growth parameters of the three vaginal lactobacilli with the four different oligosaccharides are reported in Table 4. The three strains selected were able to grow on FOS Actilight®, α-1,6/α-1,4 GOS and α-1,2/α-1,6/α-1,4 GOS as indicated by the turbidity, pH, generation time and lactate levels obtained after 48 h incubation. In contrast, very limited growth was observed on FOS Raftilose® medium whatever the strain considered.

Table 4.

Growth parameters of the three vaginal strains selected with the four different oligosaccharides after 48 h of incubation

Selected lactobacilli	**Carbohydrate**	**Growth parameters**			
		Δ_{max} T^{a}	G^{b}	Δ_{max} pH^{c}	[Lactate]^{d}
BLL 9901 *L. vaginalis*	Glucose	0.598	00:48	2.2	10.9
	FOS Actilight®	0.318	00:58	1.6	4.1
	FOS Raftilose®	0.055	01:31	0.6	1.2
	α-1,6/α-1,4 GOS	0.173	01:10	1.4	3.9
	α-1,2/α-1,6/α-1,4 GOS	0.208	01:30	1.3	3.4
BLL 2008 *L. crispatus*	Glucose	0.466	01:01	1.9	10.7
	FOS Actilight®	0.274	01:00	1.4	3.3
	FOS Raftilose®	0.083	01:24	0.6	0.0
	α-1,6/α-1,4 GOS	0.344	01:10	1.6	7.3
	α-1,2/α-1,6/α-1,4 GOS	0.262	01:13	1.2	3.0
BLL 2108 *L. jensenii*	Glucose	0.392	01:00	1.9	9.1
	FOS Actilight®	0.236	01:01	1.3	3.3
	FOS Raftilose®	0.083	01:15	0.3	0.4

Selected lactobacilli	Carbohydrate	Growth parameters			
		Δ_{max} T[a]	G[b]	Δ_{max} pH[c]	[Lactate][d]
	α-1,6/α-1,4 GOS	0.262	01:01	1.8	7.6
	α-1,2/α-1,6/α-1,4 GOS	0.345	01:06	1.3	3.3

[a] Δ_{max} T=maximal variation of turbidity at 640 nm (1/10 diluted) compared to the initial value.
[b] G=generation time (h:min).
[c] Δ_{max} pH=maximal variation of pH compared to the initial value.
[d] [Lactate]=lactate concentration at the end of fermentation (g/L).

The percentages of consumption of each oligosaccharide series (DP3 or 4) are presented in Table 5. Concerning the FOS Actilight®, oligosaccharides of DP4 to DP5 were poorly consumed whereas 80% of oligosaccharide DP3 was consumed. Concerning the α-1,6/α-1,4 GOS, all the oligosaccharides analysed of different DP, were consumed. Concerning the α-1,2/α-1,6/α-1,4 GOS, only the oligosaccharides with α-1,6 and α-1,4 bonds similar to α-1,6/α-1,4 GOS were hydrolysed. Finally, in agreement with the results obtained for growth, none of the analysed oligosaccharides of FOS Raftilose® series were metabolised.

Table 5.

Percentages of consumption of each oligosaccharide after 48 h of incubation with the lactobacilli

Carbohydrate	**Degree of polymerisation (DP)**	**Selected lactobacilli**		
		BLL 9901 *L. vaginalis*	**BLL 2008 *L. crispatus***	**BLL 2108 *L. jensenii***
Glucose	—	100	100	100
FOS Actilight®	DP3	76	76	81
	DP4	10	24	10
	DP5	10	10	10
FOS Raftilose®	DP4	10	10	10
	DP5	10	10	10
α-1,6/α-1,4 GOS	DP4[a]	37	100	100
	DP5[a]	10	94	96
	DP6[a]	10	96	94
	DP7[a]	10	93	92
α-1,2/α-1,6/α-1,4 GOS	DP4[a]	39	80	100
	DP5 (α-1,2)[b]	10	10	10
	DP5[a]	10	71	100
	DP6 (α-1,2)[b]	10	10	10

Carbohydrate	Degree of polymerisation (DP)	Selected lactobacilli		
		BLL 9901 *L. vaginalis*	**BLL 2008 *L. crispatus***	**BLL 2108 *L. jensenii***
	DP6[a]	10	36	86
	DP7[lk and lk]	10	10	47

[a] Glucooligosaccharides comprising only α-1,6 bonds after the first α-1,4 bond at the reducing end.
[b] Glucooligosaccharides comprising α-1,2/α-1,6 bonds after the first α-1,4 bond at the reducing end.

On the basis of these results, FOS Actilight® and α-1,6/α-1,4 GOS were selected for evaluation of their effect on pathogenic strains.